REMARKS

Claims 1, 5-7, 9, 11, and 27 remain in the application. Claim 1 has been amended to incorporate the subject matter of Claim 2, which has been cancelled. Specifically, Claim 1 now recites that the PPAR-gamma agonist is rosiglitazone. Since Claim 2 has been cancelled, Claim 5 has been amended to correct its dependency. No new matter has been added by way of this amendment.

The Applicants make this amendment to only expedite prosecution and do not give up the right to pursue the originally-claimed subject matter in continuing applications. Entry of this Amendment and reconsideration of this Application is respectfully requested.

35 U.S.C. §103 Rejections

The Examiner had rejected Claims 1, 2, 5-7, 9, 11, and 27 under 35 USC 103(a) as obvious over the combination of U.S. Patent No. 5,443,458 ("Eury") and WO 01/07066 (WO '066). Assuming, *arguendo*, that WO '066 is prior art, it only may be prior art under 35 U.S.C. § 102(a) as of its publication date, February 1, 2001. The concurrently-filed 37 C.F.R. §1.131 Declaration of David Ruschke and the evidence submitted therewith establish that the claimed invention was reduced to practice before February 1, 2001.

The above-identified application is assigned to MEDTRONIC AVE, INC ("assignee") and that assignment was recorded in the U.S. Patent and Trademark Office on May 6, 2002, at Reel 012871, Frame 0914. The name of assignee has since changed to Medtronic Vascular, Inc. Inventor Robert L. Cafferata no longer works for the assignee. An "assignee or other party in interest" may submit a declaration under 37 C.F.R. §1.131 "when it is not possible to produce the affidavit or declaration of the inventor."[1] David Ruschke, is the Chief Patent Counsel of Medtronic Vascular, Inc. and is authorized to execute documents on behalf of the assignee.

The Applicants have established that WO '066 is not prior art to the present application and Eury alone is insufficient to maintain the obviousness rejection. Accordingly, the Applicants respectfully request withdrawal of this rejection.

[1] MPEP 715.04 (I)(D).

35 U.S.C. §102 Rejections

The Examiner had rejected Claims 1, 5-6, and 9 under 35 USC 102(b) as being anticipated by U.S. Patent No. 5,449,382 ("Dayton"). By way of this amendment, the Applicants have incorporated Claim 2 into independent Claim 1. The Examiner did not reject Claim 2 over Dayton. Thus, Claim 1 and its dependent Claims 5-6 and 9 now must be allowable over Dayton. Accordingly, the Applicants respectfully request withdrawal of this rejection.

CONCLUSION

For the reasons discussed, the Applicants respectfully submit that all pending claims are in condition for allowance and should be passed to issue. The Commissioner is hereby authorized to charge any additional fees which may be required under 37 C.F.R. 1.17, or credit any overpayment, to Deposit Account No. 01-2525. If any issues remain, the Examiner is invited to call the undersigned at telephone (707) 543-5021.

Respectfully submitted,

/Alan M. Krubiner, Reg. No. 26,289/
Alan M. Krubiner
Registration No. 26,289
Attorney for Applicant

Medtronic Vascular, Inc.
3576 Unocal Place
Santa Rosa, CA 95403
Facsimile No.: (707) 543-5420

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appln. No.	:	10/085,539	Confirmation No.:	9853
Applicant	:	CARLYLE, Wenda		
Filed	:	February 26, 2002		
TC/A.U.	:	1616		
Examiner	:	WEBMAN, Edward J.		
Docket No.	:	P872		
Customer No.	:	28390		
Title	:	PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA LIGAND ELUTING MEDICAL DEVICE		

Mail Stop AMENDMENT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION OF DAVID RUSCHKE UNDER 37 CFR § 1.131

I, DAVID RUSCHKE, declare the following:

1. I am Chief Patent Counsel for, MEDTRONIC VASCULAR, INC.

2. I understand that the above-identified application is assigned to MEDTRONIC AVE, INC. ("ASSIGNEE") and that assignment was recorded in the U.S. Patent and Trademark Office on 06 May 2002 at Reel 012871, Frame 0914.

3. Assignee's name was changed to Medtronic Vascular, Inc. on September 9, 2003 as evidenced by Amended and Restated Certificate of Incorporation of Medtronic Ave, Inc., attached hereto as Exhibit C.

4. I am authorized to execute documents on behalf of ASSIGNEE, Medtronic Vascular, Inc..

5. I understand that in an Office Action dated 14 April 2007, the Examiner rejected Claims 1, 2, 5-7, 9, 11, and 27, of the above-identified application under 35 U.S.C. §103(a) as obvious

over the combination of U.S. Patent No. 5,443,458 and International Publication No. WO 01/07066.

6. I understand that International Publication No. WO 01/07066 was filed on 19 July 2000 and published on 1 February 2001. The cover page of International Publication No. WO 01/07066 is attached as EXHIBIT A.

7. Two redacted laboratory notebook pages of inventor Larry Cafferata, which were prepared in the United States and witnessed by Wenda Carlyle before 1 February 2001, are attached as EXHIBIT B. I understand that the laboratory notebook pages summarize and evidence the reduction to practice of the subject matter claimed in the above-identified application. EXHIBIT B, page 1, paragraph 1, describes a stent designed to improve the treatment of restenosis by eluting ligands of peroxisome proliferator-activated receptor gamma (PPARγ) from the stent. EXHIBIT B, page 1, paragraphs 2 and 6, and page 2, paragraph 1, disclose that rosiglitazone is a PPARγ ligand and is of particular interest to elute from a stent to treat restenosis.

8. All statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that the statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under 18 U.S.C. 1001, and may jeopardize the validity of this application or any patents issuing thereon.

David P. Ruschke

David Ruschke
Chief Patent Counsel,
Medtronic Vascular, Inc.

July 16, 2007

Date

EXHIBIT A

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
1 February 2001 (01.02.2001)

PCT

(10) International Publication Number
WO 01/07066 A2

(51) International Patent Classification⁷: A61K 38/00

(21) International Application Number: PCT/EP00/06986

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(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
9917405.4 23 July 1999 (23.07.1999) GB

(71) Applicant *(for all designated States except US)*: **THE UNIVERSITY OF DUNDEE** [GB/GB]; 11 Perth Road, Dundee, Tayside DD1 4HN (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **PALMER, Colin, Neil, Alexander** [GB/GB]; The University of Dundee, Biomedical Research Centre, Ninewells Hospital and Medical School, Dundee, Tayside DD1 9SY (GB). **VOSPER, Helen** [GB/GB]; The University of Dundee, Biomedical Research Centre, Ninewells Hospital and Medical School, Dundee, Tayside DD1 9SY (GB). **WOLF, Charles, Roland** [GB/GB]; The University of Dundee, Biomedical Research Centre, Ninewells Hospital and Medical School, Dundee, Tayside DD1 9SY (GB).

(74) Agent: **RUTTER, Keith**; SmithKline Beecham, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:

— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHODS OF TREATMENT AND DRUG SCREENING METHODS

(57) **Abstract:** A method of preventing or reducing foam cell development from macrophages, or removing foam cells, in a patient, the method comprising administering to the patient an effective amount of an inhibitor of PPARδ activity. A method of preventing or treating a vascular disease associated with plaque formation and/or thrombotic blockage of the blood vessels in a patient, the method comprising administering to the patient an effective amount of an inhibitor of PPARδ activity.

WO 01/07066 A2

EXHIBIT B

INVENTION: I DISCLOSE A MODIFICATION TO A STENT DESIGNED TO IMPROVE THE TREATMENT OF RESTENOSIS BY ELUTING LIGANDS OF PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR GAMMA (PPARγ) FROM THE STENT. IN ITS SIMPLEST EMBODIMENT, A SINGLE PPARγ LIGAND IS ADDED TO A STENT BEFORE IMPLANTATION IN A PHARMACEUTICALLY SUFFICIENT DOSE & WITH SUFFICIENT DURATION OF ELUTION TO BLOCK THE LOCAL INCIDENCE OF RESTENOSIS AFTER STENT DEPLOYMENT IN THE BODY.

RATIONALE FOR CHOOSING PPARγ LIGANDS: PPARγ IS A MEMBER OF A NUCLEAR RECEPTOR SUPERFAMILY THAT IS ACTIVATED BY BINDING CERTAIN LIGANDS. THESE LIGANDS CAN BE CHOSEN FROM CERTAIN FATTY ACIDS, EICOSANOIDS AND INSULIN-SENSITIZING THIAZOLIDINEDIONES. SEVERAL PHARMACEUTICAL DRUGS ARE PART OF THE LATTER CLASS: ROSIGLITAZONE, PIOGLITAZONE & TROGLITAZONE.

AN IMPORTANT CHARACTERISTIC OF ANTI-RESTENOTIC DRUGS/AGENTS IS THEIR ABILITY TO INHIBIT SMOOTH MUSCLE CELL (SMC) PROLIFERATION. PPARγ LIGANDS ARE KNOWN TO INHIBIT VASCULAR SMC PROLIFERATION PROBABLY BY DIRECT INHIBITION OF CYCLIN-DEPENDENT KINASES (1, 2).

A SECOND PROPERTY KEY IN AN ANTI-RESTENOTIC AGENT IS INHIBITION OF SMC MIGRATION (eg FROM THE MEDIA TO THE NEOINTIMA OF AN ARTERY). PPARγ LIGANDS BLOCK MIGRATION OF VASCULAR SMCs (1).

A THIRD PROPERTY FOR AN ANTI-RESTENOTIC AGENT IS ITS ABILITY TO BLOCK LOCAL INVASION/ACTIVATION OF MONOCYTES &/OR THEIR ENSUING SECRETION OF GROWTH FACTORS/CYTOKINES WHICH PRESUMABLY TRIGGER SMC ENTRY INTO THE CELL CYCLE. PPARγ AGONISTS INHIBIT ACTIVATION OF MONOCYTES (3a) & TOXINS PRODUCTION BY MONOCYTES (3b). INTERESTINGLY, IT IS KNOWN THAT CERTAIN NON-STEROIDAL ANTI-INFLAMMANT DRUGS (NSAIDs) LIKE SULINDAC ARE ANTI-RESTENOTIC IN PIGS WITH PLAQUE-LIKE LESIONS (4). THIS COULD BE RELATED TO THE FACT THAT SOME NSAIDs HAVE PPARγ AGONIST ACTIVITY AT HIGH CONCENTRATIONS (5).

RECENT CLINICAL FINDINGS DEMONSTRATE THAT PATIENTS DOSED SYSTEMICALLY WITH TROGLITAZONE HAVE REDUCED NEOINTIMAL PROLIFERATION AT SIX-MONTHS AFTER CORONARY STENT IMPLANTATION (6). UNFORTUNATELY THIS DRUG, UNDER THE TRADE NAME REZULIN, IS RECENTLY WITHDRAWN FROM USE IN TREATING TYPE II DIABETICS BECAUSE OF EXCESSIVE LIVER TOXICITY. SINCE PLASMA DRUG LEVELS WERE SIMILAR IN BOTH CASES, IT IS LIKELY THAT THE ANTI-RESTENOTIC EFFECTS OF SYSTEMIC TROGLITAZONE COULD ALSO LEAD TO

To Page No. 29

Witnessed & Understood by me,

Invented by ROBERT L. CARPENTER

Read & Understood by

DEATHS FROM LINER TOXICITY. ONE OF THE PURPOSES OF THE PRESENT INVENTION LOCALLY REDUCE THE DOSE & BIODISTRIBUTION OF THIS DRUG BY ELUTING IT FROM A STENT WITHIN THE BODY LUMEN BEING TREATED FOR RESTENOSIS.

Methods for combining pharmaceutical dosages forms onto implantable devices stents:

- PRECIPITATION, COACERVATION, CRYSTALLIZATION OF DRUG ONTO THE SURFACE OF STENT (OR WELLS/CHANNELS PLACED IN THE BODY OF THE STENT AS DRUG RESERVOIRS)
- BLENDING WITH POLYMERS THAT COAT THE SURFACES OF THE STENT (& ITS CHANNELS) & ACT AS A DIFFUSION-BARRIER TO CONTROL RELEASE OF DRUG
- ADDITION TO THE MATERIAL USED TO COMPOUND ERODIBLE POLYMERIC STENTS.
- CONTACT WITH CHEMICALLY REACTIVE SURFACES (FILMS) BONDED TO THE SURFACE OF THE STENT. ONE SUCH EXAMPLE WAS ANTICIPATED IN RAPID IN-SITU RELEASING "DRUG IMPLANT (pp 7-11).

References:

1. Law, R.E. et al. J Clin Invest 1996, 98(8): 1897-1905.
2. Wakino, S et al. J Biol Chem 2000, 275(29): 22435-41.
3a. Kintscher, U et al. Eur J. Pharmacol 2000 401(3): 259-70.
3b. USP # 5925, 657
4. Reis, E.D et al. Proc. Natl Acad Sci USA 2000 97(23): 12764-9.
5. Jiang, C et al. Nature 1998 391(6662): 82-86.
6. Takagi, T. et al. J Am Coll Cardiol 2000 36(5): 1529-35.

Witnessed & Understood by me.

Invented by Robert L. Cafferata

Recorded by

EXHIBIT C

G568

Delaware

The First State

I, HARRIET SMITH WINDSOR, SECRETARY OF STATE OF THE STATE OF DELAWARE, DO HEREBY CERTIFY THE ATTACHED IS A TRUE AND CORRECT COPY OF THE RESTATED CERTIFICATE OF "MEDTRONIC AVE, INC.", CHANGING ITS NAME FROM "MEDTRONIC AVE, INC." TO "MEDTRONIC VASCULAR, INC.", FILED IN THIS OFFICE ON THE NINTH DAY OF SEPTEMBER, A.D. 2003, AT 1:20 O'CLOCK P.M.

A FILED COPY OF THIS CERTIFICATE HAS BEEN FORWARDED TO THE NEW CASTLE COUNTY RECORDER OF DEEDS.

2269660 8100

030580192

Harriet Smith Windsor

Harriet Smith Windsor, Secretary of State

AUTHENTICATION: 2622839

DATE: 09-09-03

State of Delaware
Secretary of State
Division of Corporations
Delivered 01:19 PM 09/09/2003
FILED 01:20 PM 09/09/2003
SRV 030580192 – 2269660 FILE

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION OF MEDTRONIC AVE, INC.

Medtronic AVE, Inc., a corporation organized and existing under the General Corporation Law of the State of Delaware, hereby certifies as follows:

1. The name of the corporation is "Medtronic AVE, Inc." Its original Certificate of Incorporation was filed with the Secretary of State on July 30, 1991 under the name "Applied Vascular Engineering, Inc." Through subsequent filings with the Secretary of State, the name was changed to "Arterial Vascular Engineering, Inc." on January 30, 1996 and to "Medtronic AVE, Inc."on January 28, 1999, as the result of a merger on that date with MAV Merger Corp., which was incorporated in the State of Delaware on November 24, 1998.

2. The Amended and Restated Certificate of Incorporation of the corporation, in the form attached hereto as Exhibit A, has been duly adopted by the corporation's Board of Directors and sole stockholder in accordance with the provisions of Sections 141, 228, 242 and 245 of the General Corporation Law of the State of Delaware pursuant to unanimous written consent with waiver of meeting notice.

3. The Amended and Restated Certificate of Incorporation so approved reads in full as set forth in Exhibit A hereto and is hereby incorporated by reference herein.

IN WITNESS WHEREOF, Medtronic AVE, Inc. has caused this Certificate to be signed by David J. Scott, its Vice President and Secretary, this 8th day of September 2003.

MEDTRONIC AVE, INC.

David J. Scott, Vice President and Secretary

ATTEST:

Carol E. Malkinson, Assistant Secretary

Exhibit A

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION OF MEDTRONIC VASCULAR, INC.

ARTICLE 1 - NAME

The name of the corporation shall be Medtronic Vascular, Inc.

ARTICLE 2 - REGISTERED OFFICE AND AGENT

The registered office of the corporation in the State of Delaware is 1209 Orange Street, in the City of Wilmington, County of New Castle, Delaware, 19801. The name of its registered agent at such address is The Corporation Trust Company.

ARTICLE 3 - PURPOSES

The nature of the business or purposes to be conducted or promoted by the corporation is to engage in any lawful acts and activities for which corporations may be organized under the General Corporation Law of Delaware.

ARTICLE 4 - STOCK

The aggregate number of shares the corporation has authority to issue shall be 2,500 shares of Common Stock, $.01 par value. Holders of Common Stock shall be entitled to one vote for each share of Common Stock held of record.

ARTICLE 5 - RIGHTS OF STOCKHOLDERS

5.1) No Preemptive Rights. No holder of shares of the corporation of any class now or hereafter authorized has any preferential or preemptive right to subscribe for, purchase or receive any shares of the corporation of any class now or hereafter authorized, or any options or warrants for such shares, which may at any time be issued, sold or offered for sale by the corporation.

5.2) No Cumulative Voting Rights. No holder of shares of the corporation of any class now or hereafter authorized shall be entitled to cumulative voting.

ARTICLE 6 - MEETINGS AND BOOKS

6.1) Meetings of Stockholders and Election of Directors. Meetings of stockholders may be held within or outside the State of Delaware, as the Bylaws may provide. Elections of directors need not be by written ballot unless and except to the extent that the Bylaws so provide.

6.2) Corporate Books. The books of the corporation may be kept within or (subject to any provision contained in the statutes) outside the State of Delaware at such place or places as may be designated from time to time by the Board of Directors or in the Bylaws of the corporation.

ARTICLE 7 - LIMITATION OF DIRECTOR LIABILITY

To the fullest extent permitted by the Delaware General Corporation Law, as the same exists or may hereafter be amended, a director of the corporation shall not be liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director. If the Delaware General Corporation Law is amended after the date of the filing of this Amended and Restated Certificate of Incorporation to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the corporation shall be eliminated or limited to the fullest extent permitted by the Delaware General Corporation Law, as so amended from time to time. No repeal or modification of this Article 7 by the stockholders shall adversely affect any right or protection of a director of the corporation existing by virtue of this Article 7 at the time of such repeal or modification.

ARTICLE 8 - BYLAWS

The Board of Directors is expressly authorized to make and alter Bylaws of this corporation, subject to the power of the stockholders to change or repeal such Bylaws and subject to any other limitations on such authority provided by the General Corporation Law of Delaware.